

for the claims can be found on pages 11-15 and throughout the specification. Support for the phrase "moderate virulence" in claim 308 can be found at page 6 (figure 5 legend).

Claims 141-143, 164, 165, 167, 168 and 177 stand rejected under 35 U.S.C. §112 first paragraph. Applicants submit that this rejection is obviated in view of the new claims.

Applicants have clearly shown that NDV strains of moderate virulence (mesogenic) have anticancer properties. In the subject specification, there is an example (Example 3, page 27 along with Figure 5) of tumor regression using a strain other than 73-T: the strain MK107. MK107 is a well known mesogenic strain (Hanson and Bradley, Science 1955, 122:156-157 and Schloer and Hanson, J. Virol 1968, 2:40-47). Further, in commonly owned U.S. Serial No. 09/292,376, there are examples of antitumor efficacy with two other mesogenic strains of NDV in Examples 21, 22, 23. This is in addition to the extensive examples (Examples 1-10, 16-17, 29 and including an example with human clinical data- Example 20) that used MK107, the known mesogenic strain.

Various modes of administration are clearly enabled in the specification. See Example 2 (page 26): "Treatment of human tumors in athymic mice using systemic NDV therapy." In this example intraperitoneal treatment using NDV led to complete tumor regression of 6 of 7 tumors located subcutaneously on the flank. The legend to Figure 4 (for which this example refers) on page 6 also clearly indicates that these are "systemic" injections: "Figure 4 shows regression of IMR-32 human neuroblastoma xenografts following systemic (intraperitoneal) injections of live NDV (strain 73-T)."

In commonly owned Serial No. 09/292,376, additional examples are provided of antitumor efficacy using systemic treatment (in this case by the intravenous route) with

mesogenic MK107 strain: Examples 3, 9 and 20 (with Example 20 showing clinical human experience of systemic treatment including regressions of 5 tumors).

Claims 141-143, 164, 165, 167, 168 and 177 stand rejected under: 35 U.S.C. §102(b) as being anticipated by Lorence et al. Reconsideration is requested.

Use of a mesogenic strain or a strain of "moderate virulence" (see new claim 308) is not taught in Lorence et al (1988). Lorence et al (1988) only uses strain 73-T for in vitro tumor data - there is no in vivo data and no data on dosing and dosages. Strain 73-T used in this 1988 paper for all tumor cell experimentation is a strain of high virulence in contrast to MK107 which is of moderate virulence (see the subject specification, Figure 5 legend on page 6).

Claims 141-143, 164, 165, 167, 168 and 177 stand rejected under 35 U.S.C. §102(a) as being anticipated by Reichard et al; and rejected under 35 U.S.C. §102(b) as being anticipated by Reichard et al. Reconsideration is requested.

Applicants submit that these rejections are obviated in view of the new claims. Reichard et al (1992) as in the Lorence 1988 paper only use the 73-T strain for studies using tumor cells. As indicated in the arguments above, this paper does not teach the use of a strain of "moderate virulence" (see new claim 308).

Further, in Reichard, mammals with cancer were not treated; instead tumor cells were injected subcutaneously into mice followed immediately by injection of virus into the subcutaneous wheal where the tumor cells were injected. See paragraph bridging pages 449-450 of Reichard et al. This is in contrast to the subject claims for treating cancer in a mammal having cancer.

In addition, the dose used in the present application to treat established cancers is at least ten times greater than that used in Reichard et al for the administration of tumor cells and virus (at least 1×10^7 PFU per mouse per injection versus 1×10^6 PFU per mouse per injection in Reichard et al). This dose of 1×10^7 PFU per mouse is approximately 4×10^8 PFU per kilogram body weight, assuming a 25 gram mouse. This is the dose for intralesional administration of NDV to treat established cancers. For systemic administration, a dose that is 10-fold higher is required. See Example 2 of the subject application. Also, see generally page 13, lines 13-35 and Examples 1-3 and 5 of the subject application. The use of these much higher doses is not taught or suggested by Reichard et al. Indeed, the use of these higher doses is contrary to the teachings of Reichard et al which suggests that only a small number of NDV will be necessary for systemic treatment of tumors (see lines 2-4 from the bottom of the first column on page 452 of Reichard et al).

The viral strains of the subject application are less virulent strains than the 73T strain used in Reichard et al (see Example 3 of the subject application). There is nothing in Reichard et al to teach or suggest that a less virulent strain would be effective in treating cancer.

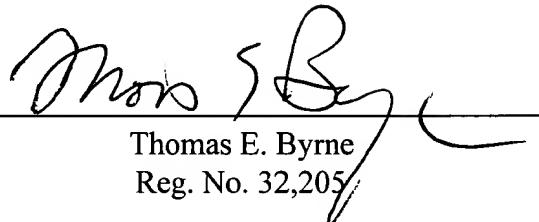
Should any small matters remain outstanding, Examiner Scheiner is encouraged to telephone Applicants' undersigned attorney at 387-3008 so that same can be resolved without the necessity of an additional action and response thereto.

Robert M. LORENCE et al
Serial No. 08/260,536

Respectfully submitted,

NIXON & VANDERHYE P.C.

By:


Thomas E. Byrne
Reg. No. 32,205

TEB:lmo
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100